

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 21779

**Title:** Generation of diverse neural cell types through direct conversion

**Reviewer's code:** 02446119

**Reviewer's country:** China

**Science editor:** Shui Qiu

**Date sent for review:** 2015-08-01 16:12

**Date reviewed:** 2015-08-08 13:56

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[ Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[ Y] No	

## COMMENTS TO AUTHORS

This review comprehensively summarized current concepts and practical methods to converse somatic cells into neural cells, which is an important advantage in stem cell manipulation and potential clinical application. It is a well organized manuscript and is helpful to understand the advance in this research field. Reading the fluent language is a joyful thing in addition to its scientific description. I am not sure if the English style spelling of some words is acceptable for the journal.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 21779

**Title:** Generation of diverse neural cell types through direct conversion

**Reviewer's code:** 02446101

**Reviewer's country:** China

**Science editor:** Shui Qiu

**Date sent for review:** 2015-08-01 16:12

**Date reviewed:** 2015-10-15 23:53

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

First of all, this manuscript is a review. You described the generation of diverse neural cell types via direct conversion of somatic cells, with comparison against stem cell-based approaches, as well as discussion of their potential research and clinical applications. And I found no similar published paper. So, this manuscript has a certain degree of innovation. Secondly, the repair of the damaged nerve is always a hotspot both in clinical research and basic research. You not only gathered most of the scattered papers on this field and provides readers the current progress in understanding the generation of neural cell types via direct conversion, but also compared it with stem cell-based approaches and discussed the trend of development, which is very helpful to the following researchers. What's more, your language is appropriate. As suggested above, I agree to accept this manuscript.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**ESPS manuscript NO:** 21779

**Title:** Generation of diverse neural cell types through direct conversion

**Reviewer's code:** 02446120

**Reviewer's country:** Argentina

**Science editor:** Shui Qiu

**Date sent for review:** 2015-08-01 16:12

**Date reviewed:** 2015-10-21 21:52

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Comments to authors: The manuscript, "Generation of diverse neural cell types through direct conversion", a review by "G Petersen and P. Strappe", discusses different ways of obtaining neuronal cells from stem cells, and compares the advantages and disadvantages of these methods with the direct conversion of various cell types into neuronal cells. Currently, due to the overwhelming advances in stem cell research, there are many possible ways of obtaining cells for repairing tissues, however their potential therapeutic application is hampered by many ethical and methodological concerns, and for the still high risk that the replacement cells may transform into cancer cells. In general, the work is relevant since it analyses the main problems regarding the use of stem cells along with the "pros" and "contras" of their possible utilization in clinic. The manuscript is interesting, clear and easy to read and understand and it has an extensive and adequate bibliography. In fact, the present review would enlighten our understanding of stem cells. Major concerns: - Pag 5: "Induced Pluripotent Stem Cells.." Authors: Regarding the therapeutic use of stem cells, a protocol was recently approved in Japan for injecting stem cells in a patient suffering from Macular degeneration. It would be important that the authors include a paragraph discussing this

important issue - Pag 7: "Induced Pluripotent Stem Cells... supplementation with a range of chemicals including  $\beta$ -mercaptoethanol, butylated hydroxyanisole, dimethylsulphoxide, isobutylmethylxanthine, dibutyryl cyclic AMP, epidermal growth factor, and brain-derived neurotrophic factor.." The authors should expand this topic, since as it is now is a simple list of compounds used to transform adult cells into stem cells with no discussion or analysis. - Pag 7: "Generation of Neural Cell Types via Direct Conversion..." Authors: One of the main problems related to a direct conversion of neuronal cells is that to repair the damaged tissues it is required not only to transform a given cell type into a neuron, but also to generate a significant number of cells by activation of cell cycle progression. It would be necessary that the authors comment this topic. -Pag 9 "The Beginnings of Neural Direct Conversion.. "Other studies have also investigated microRNA-mediated direct conversion in conjunction with neuronal specific transcription factors, through expression of microRNA-9/9\* and microRNA-124, which are known to act on critical target genes that regulate neuronal differentiation and function" The authors should add a paragraph indicating more clearly the possible roles of these and other miRNA as well. - Comparing with other regions of the central nervous system, the retina is a tissue of easy access and therefore appropriate for therapeutic intervention with stem cells, therefore it would be necessary that the authors include a paragraph discussing the possible regeneration of retinal neurons in patients with eye diseases. End of comments